Important Advances in Clinical Medicine

Epitomes of Progress — Internal Medicine

The Scientific Board of the California Medical Association presents the following inventory of items of progress in internal medicine. Each item, in the judgment of a panel of knowledgeable physicians, has recently become reasonably firmly established, both as to scientific fact and important clinical significance. The items are presented in simple epitome and an authoritative reference, both to the item itself and to the subject as a whole, is generally given for those who may be unfamiliar with a particular item. The purpose is to assist the busy practitioner, student, research worker or scholar to stay abreast of these items of progress in internal medicine which have recently achieved a substantial degree of authoritative acceptance, whether in his own field of special interest or another.

The items of progress listed below were selected by the Advisory Panel to the Section on Internal Medicine of the California Medical Association and the summaries were prepared under its direction.

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Digoxin, Quinidine and Sudden Death

THE INTRODUCTION OF QUINIDINE into clinical practice in 1918 marked the beginning of effective therapy for cardiac arrhythmias. The use of quinidine to convert atrial filbrillation to sinus rhythm, however, was associated with a high incidence of sudden death (estimated at between 2 percent and 4 percent). This phenomenon of quinidine syncope occurred almost entirely in patients who were also receiving digitalis. An explanation for this phenomenon has recently been discovered: Addition of quinidine to digoxin therapy causes a dramatic increase in levels of digoxin in the blood.

Levels of the drug in the body are initially determined by body size (volume of distribution) and at steady state by elimination processes (clearance). In a typical patient taking digoxin, about 50 percent of the daily dose is excreted in the urine; the reminder is cleared by metabolic and fecal loss. Quinidine decreases the volume of distribution of digoxin by displacing it from tissue binding sites. This leads to a rapid rise in digoxin concentration and an increase in cardiac effect. Quinidine also quickly decreases the elimination of digoxin by both renal and nonrenal routes, leading to a twofold increase in the drug's concentration over a week's time. The combined effects of decreased tissue binding and impaired clearance cause an immediate and sustained elevation of digoxin levels in the body.

Cardiac toxicity may be a consequence of this raised level alone; however, this condition is made more severe by quinidine-induced prolongation of ventricular repolarization (shown by prolonged QT interval), leading to ventricular tachyarrhythmias, syncope and sudden death.

The pharmacokinetic interaction also occurs between digitoxin and quinidine, but not with procainamide or disopyramide. Patients with renal impairment may be particularly at risk because they rely almost entirely on nonrenal elimination of digoxin, which is virtually abolished by the action of quinidine. It would seem prudent to stop digoxin therapy for two days after starting quini-

dine, and then to resume administration at half the original dose if digoxin levels are to remain the same. The serum concentration should be checked after the patient has been on the new regimen for a week.

Quinidine-digoxin toxicity should be treated by discontinuing administration of both drugs. The rapid elimination of quinidine will lead to a fall in digoxin concentration as the volume of distribution of digoxin increases. Lidocaine, bretylium and overdrive-pacing have proved effective in treating arrhythmias, but drugs which prolong the QT interval, such as procainamide and disopyramide should be avoided.

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REFERENCES

Reynolds EW, Vander Ark CR: Quinidine syncope and the delayed repolarization syndromes. Mod Concepts Cardiovasc Dis 45: 117-122, Aug 1976

Chapron DJ, Mumford D, Pitegoff GI: Apparent quinidine-induced digoxin toxicity after withdrawal of pentobarbital: A case of sequential drug interactions. Arch Intern Med 139:363-365, Mar 1979

Hager WD, Fenster P, Mayersohn M, et al: Digoxin-quinidine interaction—Pharmacokinetic evaluation. N Engl J Med 300:1238-1241, May 31, 1979

Prescribing Exercise

INDICATIONS FOR RESTRICTING ACTIVITY until recently have been more clearly defined than indications for exercise. From data accumulated over the past 20 years, guidelines for prescribing exercise have been developed.

A patient's history, findings on physical examination and a multistage exercise test (MSET) form the basis from which an exercise prescription is determined. From the MSET the target heart rate for exercise (peak heart rate and the maximum work load) is derived and the patient can be advised of other activities of equivalent workload which he or she can safely carry out.

The exercise prescription should specify the frequency, intensity, duration and type of exercise. A minimum of three days of exercise a week, preferably nonconsecutive days, is necessary. High-intensity exercise is neither enjoyable nor safe for cardiac patients. Each patient should be advised to exercise to maintain a heart rate of 70 percent to 85 percent that achieved on the MSET. The exercise most easily undertaken, most readily monitored and most often prescribed is walking. Other endurance activities such as jogging, cycling and swimming can also be prescribed.

The usual exercise session should last about an hour, with 10 minutes of warm-up, 20 to 50 minutes of endurance exercise and 5 to 10 minutes of cool-down. The warm-up and cool-down periods are important and should not be omitted because they serve to develop and maintain flexibility and muscle strength as well as reducing the risk of muscle problems, injuries and fatigue.

A patient's initial level of fitness and clinical status are important considerations when developing the exercise prescription. Typically, an asymptomatic patient who seeks advice concerning exercise is over 40 years old, has a major coronary risk factor or suspected coronary artery disease and has been inactive for some years. Therefore, initial exercise sessions should be short and more frequent. Patients with established cardiac disease or a chronic illness will also need a slow initiation into exercise and special attention to medications that may affect such exertion. Early low-level treadmill testing and exercise for patients after myocardial infarction and myocardial revascularization operations are safe and advantageous. Periodic review and repeat MSE testing are required to adjust the target heart rate with exercise.

Exercise is a lifelong commitment and is most valuable when it is a component of a treatment program that deals with all the cardiovascular risk factors that can be modified or controlled.

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REFERENCES

Erb BD, Fletcher GF, Sheffield TL: Standards for cardiovascular exercise treatment programs (AHA Committee Report). Circulation 59:1084A-1090A, May 1979

Fox SM 3rd, Naughton JP, Gorman PA: Physicial activity and cardiovascular health—Part 1. Potential for prevention of coronary heart disease and possible mechanisms; Part 2. The exercise prescription—Intensity and duration; Part 3. The exercise prescription—Frequency and type of activity. Mod Concepts Cardiovasc Dis 41:17-20, 21-24, 25-30, Apr, May, Jun 1972

Hanson PG, Giese MD, Corliss RJ: Clinical guidelines for exercise training. Postgrad Med 67:120-138, Jan 1980

Intracavitary Electrodes for Diagnosis and Treatment of Arrhythmias

ALTHOUGH SEVERAL ARTICLES have reported the use of right atrial intracavitary electrode electrogram monitoring and therapeutic pacing for diagnosis and treatment of atrial arrhythmias, this modality unfortunately has had limited use.

It is well recognized that an arrhythmia such as atrial flutter with 2:1 atrial ventricular conduction may be extremely difficult to diagnose. This form of atrial flutter may be confused with sinus, atrial or junctional tachycardia. If aberrant ventricular conduction is present, confusion with ven-